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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 7	AUG 27	USPATOLD now available on STN
NEWS 8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 10	SEP 13	FORIS renamed to SOFIS
NEWS 11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 16	OCT 19	BEILSTEIN updated with new compounds
NEWS 17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 18	NOV 19	WPIX enhanced with XML display format
NEWS 19	NOV 30	ICSD reloaded with enhancements
NEWS 20	DEC 04	LINPADOCDB now available on STN
NEWS 21	DEC 14	BEILSTEIN pricing structure to change
NEWS 22	DEC 17	USPATOLD added to additional database clusters
NEWS 23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 24	DEC 17	DGENE now includes more than 10 million sequences
NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 29	JAN 02	STN pricing information for 2008 now available
NEWS 30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 31	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 32	JAN 28	MARPAT searching enhanced
NEWS 33	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 34	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 35	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,

CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:06:24 ON 04 FEB 2008

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.84	0.84

FILE 'REGISTRY' ENTERED AT 13:08:35 ON 04 FEB 2008
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STRUCTURE FILE UPDATES: 3 FEB 2008 HIGHEST RN 1001389-12-3
DICTIONARY FILE UPDATES: 3 FEB 2008 HIGHEST RN 1001389-12-3

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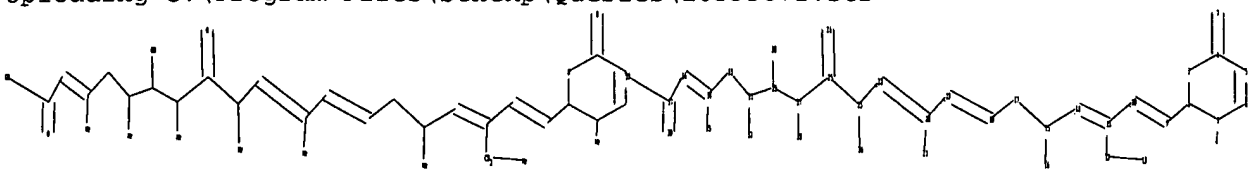
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10535672.str



chain nodes :
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
29 30 31 32 33 34 35 36 37 38 39

```
ring nodes :
1  2  3  4  5  6
chain bonds :
1-8  2-9  4-7  9-10  10-11  11-12  11-14  12-13  14-15  15-16  15-17  17-18  18-19
19-20  20-21  20-22  22-23  23-24  23-25  25-26  25-27  27-28  27-29  29-30  29-31
31-32  31-33  33-34  34-35  34-36  36-37  37-38  37-39
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
4-7  25-26  29-30
exact bonds :
1-2  1-6  1-8  2-3  2-9  3-4  4-5  5-6  9-10  10-11  11-12  11-14  12-13  14-15
15-16  15-17  17-18  18-19  19-20  20-21  20-22  22-23  23-24  23-25  25-27  27-28
27-29  29-31  31-32  31-33  33-34  34-35  34-36  36-37
normalized bonds :
37-38  37-39
isolated ring systems :
containing 1 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:CLASS
 11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS
19:CLASS  20:CLASS  21:CLASS  22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS
27:CLASS  28:CLASS  29:CLASS  30:CLASS  31:CLASS  32:CLASS  33:CLASS  34:CLASS
35:CLASS  36:CLASS  37:CLASS  38:CLASS  39:CLASS



L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 13:09:01 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        4 TO ITERATE

100.0% PROCESSED        4 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            4 TO      200
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 13:09:06 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       69 TO ITERATE

100.0% PROCESSED       69 ITERATIONS                                  7 ANSWERS
SEARCH TIME: 00.00.01

L3            7 SEA SSS FUL L1

=> file caplus
```

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.36	179.20

FILE 'CAPLUS' ENTERED AT 13:09:26 ON 04 FEB 2008
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FILE COVERS 1907 - 4 Feb 2008 VOL 148 ISS 6
FILE LAST UPDATED: 3 Feb 2008 (20080203/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3 full
L4 144 L3

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.48	179.68

FILE 'REGISTRY' ENTERED AT 13:09:47 ON 04 FEB 2008
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STRUCTURE FILE UPDATES: 3 FEB 2008 HIGHEST RN 1001389-12-3
DICTIONARY FILE UPDATES: 3 FEB 2008 HIGHEST RN 1001389-12-3

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s l3
SAMPLE SEARCH INITIATED 13:09:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

```
100.0% PROCESSED         4 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:             4 TO      200
PROJECTED ANSWERS:                0 TO        0

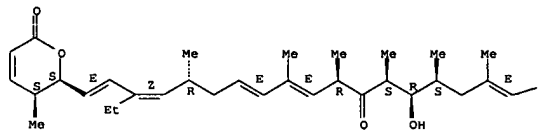
L5            0 SEA SSS SAM L1

=> d scan l3
```

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 2,10,12,16,18-Nonadecapentaenoic acid,
19-[(2S,3S)-3,6-dihydro-3-methyl-6-
oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
monosodium salt, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (9CI)
MF C33 H48 O6 . Na

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



● Na

PAGE 1-B

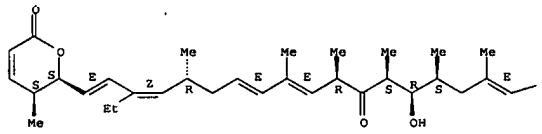
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 2,10,12,16,18-Nonadecapentaenoic acid, 19-(3,6-dihydro-3-methyl-6-oxo-2H-
pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, compd.
with N,N-diethylethanamine (1:1) (9CI)
MF C33 H48 O6 . C6 H15 N

CM 1

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

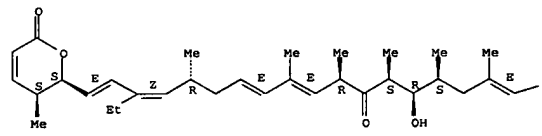
CM 2

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 2,10,12,16,18-Nonadecapentaenoic acid,
19-[(2S,3S)-3,6-dihydro-3-methyl-6-
oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
(2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)-
MF C33 H48 O6
CI COM

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

```
=>  file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         3.68     183.36

FILE 'CAPLUS' ENTERED AT 13:14:43 ON 04 FEB 2008
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COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)
```



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FILE COVERS 1907 - 4 Feb 2008  VOL 148 ISS 6
FILE LAST UPDATED: 3 Feb 2008  (20080203/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3 full
L6          144 L3

=> s l6 and leptomycin?
            647 LEPTOMYCIN?
L7          136 L6 AND LEPTOMYCIN?

=> s l7 and metalloproteinas?
          29028 METALLOPROTEINAS?
L8            2 L7 AND METALLOPROTEINAS?

=> s l7 and leptomycin B
            645 LEPTOMYCIN
             11 LEPTOMYCINS
            646 LEPTOMYCIN
                  (LEPTOMYCIN OR LEPTOMYCINS)
        1750615 B
            618 LEPTOMYCIN B
                  (LEPTOMYCIN(W)B)
L9          136 L7 AND LEPTOMYCIN B

=> s l9 and py<2002
       21937595 PY<2002
L10           55 L9 AND PY<2002

=> s l10 and skin
          272623 SKIN
           10809 SKINS
          278708 SKIN
                  (SKIN OR SKINS)
L11            0 L10 AND SKIN
```

```
=> s l10 and fungal
         56895 FUNGAL
            15 FUNGALS
         56902 FUNGAL
                  (FUNGAL OR FUNGALS)
L12           1 L10 AND FUNGAL

=> d ibib abs hitstr tot
```

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:94109 CAPLUS
DOCUMENT NUMBER: 128:215353
TITLE: Microbial conversion products of leptomycin B
AUTHOR(S): Kuhnt, Michaela; Bitsch, Francis; Ponelle, Monique; Sanglier, Jean-Jacques; Wang, Ying; Wolff, Barbara
CORPORATE SOURCE: Core Technology Area, Research, Novartis Pharma Inc., Basel, CH-4002, Switz.
SOURCE: Applied and Environmental Microbiology (1998), 64(2), 714-720
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:215353

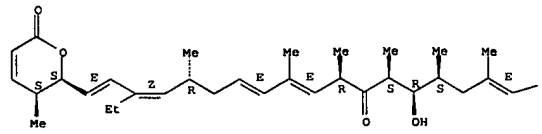
AB Leptomycin B (LMB), a secondary metabolite produced by Streptomyces sp. strain ATS 1287 with known antifungal and antitumor effects, inhibits the nucleo-cytoplasmic translocation of the human immunodeficiency virus type 1 regulatory protein Rev and exhibits significant antiproliferative activity. Since LMB itself turned out to be distinctly cytotoxic, a bioconversion screening with a selected set of 29 bacterial and 72 fungal strains was performed in order to obtain metabolites of LMB with reduced antiproliferative effects. Several derivs. of LMB, more polar than the parent compound and produced in yields of >5%, were detected. Liquid chromatog.-mass spectroscopy anal. indicated the type of bioconversion. Fermns. (1 L scale) of those strains with high rates of transformation were suitable for isolation and characterization of the most prominent metabolites. Thus, bioconversion of LMB with Aspergillus flavus ATCC 9170 and Emericella unguis ATCC 13431 served for isolation of the novel derivs. 26-hydroxy-LMB (30% was the concentration of the metabolite [with respect to LMB] used for bioconversion) and LMB-24-glutaminamide (90%), resp. Streptomyces rimosus ATCC 28893 converted LMB into 4,11-dihydroxy-LMB (13%) and 2,3-dihydro-LMB (55%). Although the antiproliferative effects of the LMB metabolites could be reduced through microbial conversion, none of these metabolites inhibited the nuclear export of Rev better than LMB itself.

IT 87081-35-4, Leptomycin B
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(microbial leptomycin B metabolites as proliferation inhibitors)

RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

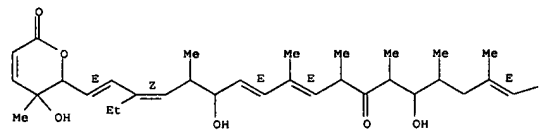
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS FORMAT
RECORD. ALL CITATIONS AVAILABLE IN THE RE



IT 204330-96-1, 4,11-Dihydroxyleptomycin B
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(microbial leptomycin B metabolites as proliferation inhibitors)

RN 204330-96-1 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-(3,6-dihydro-3-hydroxy-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6,14-dihydroxy-3,5,7,9,11,15-hexamethyl-8-oxo- (9CI) (CA INDEX NAME)

Double bond geometry as shown.
Currently available stereo shown.



```
=> s l10 and tumor
        438664 TUMOR
        165222 TUMORS
        489727 TUMOR
                  (TUMOR OR TUMORS)
L13           7 L10 AND TUMOR

=> d ibib abs hitstr tot
```

L13 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:829425 CAPLUS
DOCUMENT NUMBER: 136:80081
TITLE: Dynamics of leptomycin B-sensitive nucleocytoplasmic flux of parathyroid hormone-related protein
AUTHOR(S): Lam, Mark H. C.; Henderson, Beric; Gillespie, Matthew T.; Jans, David A.
CORPORATE SOURCE: Nuclear Signalling Laboratory, Division of Biochemistry and Molecular Biology, John Curtin School of Medical Research, Canberra, Australia
SOURCE: Traffic (Copenhagen, Denmark) (2001), 2(11), 812-819
CODEN: TRAFFA; ISSN: 1398-9219
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Parathyroid hormone-related protein is responsible for hypercalcemia induced by various tumors. The similarity of its N-terminus to that of parathyroid hormone enables parathyroid hormone-related protein to share parathyroid hormone's signaling properties, but the rest of the mol. possesses distinct functions including a role in the nucleus/nucleolus in reducing apoptosis and enhancing cell proliferation. We have previously shown that parathyroid hormone-related protein nuclear import is mediated by importin β1. Here we use fluorescence recovery after photobleaching for the first time to show that, in living cells, parathyroid hormone-related protein is exported from the nucleus in a leptomycin B-sensitive manner, implicating CRM1 as the parathyroid hormone-related protein nuclear export receptor. Leptomycin B treatment significantly reduced the rate of nuclear export 4 -10-fold, thereby increasing parathyroid hormone-related protein concentration in the nucleus/nucleolus about 2-fold. Intriguingly, this also led to a 2-fold reduced nuclear import rate. Inhibiting the nuclear export of a protein able to shuttle between nucleus and cytoplasm through distinct receptors thus can also affect nuclear import, indicating that the subcellular localization of a protein containing distinct nuclear import and export signals is the product of an integrated system. Although there have been several recent studies examining the dynamics of intranuclear transport using fluorescence recovery after photobleaching, this represents, to our knowledge, the first use of the technique to examine the kinetics of nucleocytoplasmic flux in living cells.

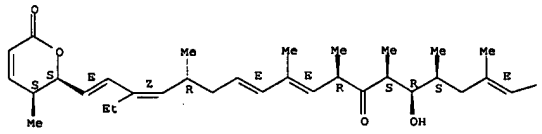
IT 87081-35-4, Leptomycin B
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(parathyroid hormone-related protein leptomycin B -sensitive nucleocytoplasmic flux and dynamics thereof)

RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L13 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:815253 CAPLUS
DOCUMENT NUMBER: 136:49258
TITLE: Suppressor of fused negatively regulates β-catenin signaling
AUTHOR(S): Meng, Xianwang; Poon, Raymond; Zhang, Xiaoyun; Cheah, Alexander; Ding, Qi; Hui, Chi-Chung; Alman, Benjamin
CORPORATE SOURCE: Program in Developmental Biology, The Hospital for Sick Children, University of Toronto, Toronto, ON, M5G1X8, Can.
SOURCE: Journal of Biological Chemistry (2001), 276(43), 40113-40119
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

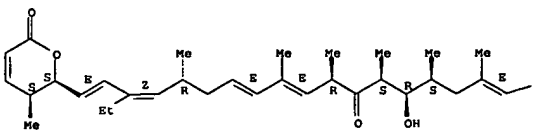
AB Suppressor of fused (Su(fu)) is a neg. regulator of the Hedgehog signaling pathway that controls the nuclear-cytoplasmic distribution of Gli/Ci transcription factors through direct protein-protein interactions. We show here that Su(fu) is present in a complex with the oncogenic transcriptional activator β-catenin and functions as a neg. regulator of T-cell factor (Tcf)-dependent transcription. Overexpression of Su(fu) in SW480 (APCmut) colon cancer cells in which β-catenin protein is stabilized leads to a reduction in nuclear β-catenin levels and in Tcf-dependent transcription. This effect of Su(fu) overexpression can be blocked by treatment of these cells with leptomycin B, a specific inhibitor of CRM1-mediated nuclear export. Overexpression of Su(fu) suppresses growth of SW480 (APCmut) tumor cells in nude mice. These observations indicate that Su(fu) neg. regulates β-catenin signaling and that CRM-1-mediated nuclear export plays a role in this regulation. Our results also suggest that Su(fu) acts as a tumor suppressor.

IT 87081-35-4, Leptomycin B
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(suppressor of fused neg. regulates β-catenin signaling)

RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



L13 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-B

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:780361 CAPLUS
DOCUMENT NUMBER: 134:82300
TITLE: Adenomatous polyposis coli protein contains two nuclear export signals and shuttles between the nucleus and cytoplasm
AUTHOR(S): Neufeld, Kristi L.; Nix, David A.; Bogerd, Hal; Kang, Yibin; Beckerle, Mary C.; Cullen, Bryan R.; White, Raymond L.
CORPORATE SOURCE: Department of Oncological Sciences, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(22), 12085-12090
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mutational inactivation of the adenomatous polyposis coli (APC) tumor suppressor initiates most hereditary and sporadic colon carcinomas. Although APC protein is located in both the cytoplasm and the nucleus, the protein domains required to maintain a predominantly cytoplasmic localization are unknown. Here, we demonstrate that nuclear export of APC is mediated by two intrinsic, leucine-rich, nuclear export signals (NESs) located near the amino terminus. Each NES was able to induce the nuclear export of a fused carrier protein. Both APC NESs were independently able to interact with the Crm1 nuclear export factor and substitute for the HIV-1 Rev NES to mediate nuclear mRNA export. Both APC NESs functioned within the context of APC sequence: an amino-terminal APC peptide containing both NESs interacted with Crm1 and showed nuclear export in a heterokaryon nucleocytoplasmic shuttling assay. Also, mutation of both APC NESs resulted in the nuclear accumulation of the full-length, .apprx.320-kDa APC protein, further establishing that the two intrinsic APC NESs are necessary for APC protein nuclear export. Moreover, endogenous APC accumulated in the nucleus of cells treated with the Crm1-specific nuclear export inhibitor leptomycin B. Together, these data indicate that APC is a nucleocytoplasmic shuttle protein whose predominantly cytoplasmic localization requires NES function and suggests that APC may be important for signaling between the nuclear and cytoplasmic compartments of epithelial cells.

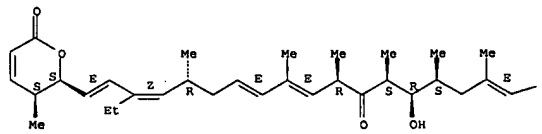
IT 87081-35-4, Leptomycin B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(nuclear export inhibitor leptomycin B blocks APC protein transport to cytoplasm)

RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L13 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:525399 CAPLUS
DOCUMENT NUMBER: 133:217377
TITLE: Activation of p53 in cervical carcinoma cells by small molecules
AUTHOR(S): Hietanen, Sakari; Lain, Sonia; Krausz, Eberhard; Blattner, Christine; Lane, David P.
CORPORATE SOURCE: CRC Cell Transformation Group, Department of Biochemistry, University of Dundee, Dundee, DD1 5EH, UK
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(15), 8501-8506
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In over 90% of cervical cancers and cancer-derived cell lines, the p53 tumor suppressor pathway is disrupted by human papillomavirus (HPV). The HPV E6 protein promotes the degradation of p53 and thus inhibits the stabilization and activation of p53 that would normally occur in response to HPV E7 oncogene expression. Restoration of p53 function in these cells by blocking this pathway should promote a selective therapeutic affect. Here we show that treatment with the small mol. nuclear export inhibitor, leptomycin B, and actinomycin D leads to the accumulation of transcriptionally active p53 in the nucleus of HeLa, CaSki, and SiHa cells. Northern blot analyses showed that both actinomycin D and leptomycin B reduced the amount of HPV E6-E7 mRNA whereas combined treatment with the drugs showed almost complete disappearance of the viral mRNA. The combined treatment activated p53-dependant transcription, and increases in both p21WAF1/CIP1 and Hdm2 mRNA were seen. The combined treatment resulted in apoptotic death in the cells, as evidenced by nuclear fragmentation and PARP-cleavage indicative of caspase 3 activity. These effects were greatly reduced by expressing a dominant neg. p53 protein. The present study shows that small mols. can reactivate p53 in cervical carcinoma cells, and this reactivation is associated with an extensive biol. response, including the induction of the apoptotic death of the cells.

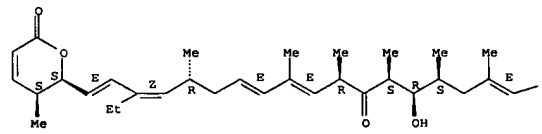
IT 87081-35-4, Leptomycin B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activation of p53 in cervical carcinoma cells by small mols.)

RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L13 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:9882 CAPLUS
DOCUMENT NUMBER: 132:146316
TITLE: Effects on normal fibroblasts and neuroblastoma cells of the activation of the p53 response by the nuclear export inhibitor leptomycin B
AUTHOR(S): Smart, Philip; Lane, E. Birgitte; Lane, David P.; Midgley, Carol; Vojtesek, Borek; Lain, Sonia
CORPORATE SOURCE: CRC Cell Transformation Group, Department of Biochemistry, MSI/WTB, University of Dundee, Dundee, DD1 5EH, UK
SOURCE: Oncogene (1999), 18(51), 7378-7386
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

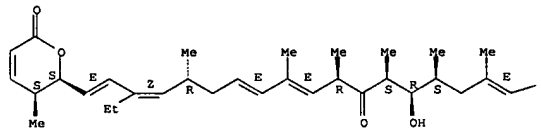
AB P53 tumor suppressor protein levels and p53-dependent transcriptional activity have been recently shown to increase in cells treated with leptomycin B (LMB), an inhibitor of nuclear export. Expts. presented here show that LMB treatment leads to growth arrest and a senescence-like phenotype in human normal fibroblast cultures. This effect is reversible after removal of the drug and further passage by trypsinization. Instead, LMB has a strong cytotoxic effect on human neuroblastoma cell lines even at nanomolar concns. In both these cell types the effects of LMB are attenuated when the activity of the endogenous wild type p53 protein is abrogated by overexpression of a dominant neg. p53 mutant. We conclude that the induction of the p53 response by LMB plays an important role in the effects of this drug on cultured cells.

IT 87081-35-4, Leptomycin B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of activation of the p53 response by leptomycin B on normal fibroblasts and neuroblastoma cells)

RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



L13 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-B

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:451496 CAPLUS
DOCUMENT NUMBER: 107:51496
TITLE: Studies on the new antibiotics kazusamycin and related substances
AUTHOR(S): Umezawa, Iwao; Komiyama, Kanki
CORPORATE SOURCE: Kitasato Inst., Japan
SOURCE: Gan to Kagaku Ryoho (1987), 14(3, Pt. 2), 859-64
CODEN: GTKRDX; ISSN: 0385-0684
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

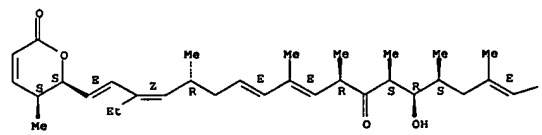
AB Kazusamycins A and B and leptomycin B have a structure characteristic of an unsatd., branched-chain fatty acid with a terminal δ-lactone ring, and the former 2 agents show antimicrobial activity on some kinds of fungi. Kazusamycin A (KZM-A) showed cytotoxic activity on mammalian cells at very low concns. (nanogram per mL range) in vitro. The antibiotic inhibited not only the growth of transplantable murine tumors and their metastases to the lung but also human mammary tumors inoculated into nude mice. KZM-A was rapidly distributed to the main organs of mice, and a percentage of the antibiotic was inactivated by binding to high-mol.-weight substances such as albumin. A large quantity of KZM-A was carried to the liver and excreted into the bile, but was then reabsorbed by the small intestine. The growth of tumor metastases (L5178Y cells) in the liver was suppressed by KZM-A. The antibiotic induced severe diarrhea by causing necrosis and(or) lysis of the mucous membrane of the small intestine. In contrast to this, the degree of myelotoxicity was relatively slight. The active site of the fatty acid of KZM-A appeared to consist of conjugated double bonds, carboxylic acid, and hydroxyl moieties.

IT 87081-35-4, Leptomycin B
RL: PRP (Properties)
(antimicrobial and antitumor effects of)

RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



L13 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

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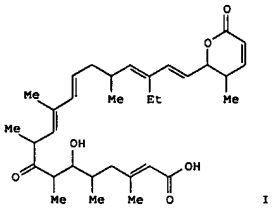
L13 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:214721 CAPLUS
DOCUMENT NUMBER: 102:214721
ORIGINAL REFERENCE NO.: 102:33527a,33530a
TITLE: Antitumor activity of leptomycin B
AUTHOR(S): Komiyama, Kanki; Okada, Kenji; Tomisaka, Shigeru; Umezawa, Iwao; Hamamoto, Tetsuo; Beppu, Teruhiko
CORPORATE SOURCE: Kitasato Inst., Tokyo, 108, Japan
SOURCE: Journal of Antibiotics (1985), 38(3), 427-9
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

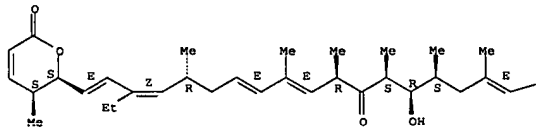
AB Leptomycin B (I) [87081-35-4] increased the life span of mice bearing Erlich ascites tumors and Lewis lung carcinoma, but had only slight effects in mice bearing B-16 melanoma and P-388 lymphatic leukemia. I inhibited the growth of HeLa cells at a concentration of 4.9 ng/mL when the cells were exposed for 3 days. When HeLa cells were exposed to I for 3 days, many polynuclear giant cells and masses of small nuclei appeared at a concentration of 1.25-2.5 ng/mL. Thus, the antitumor activity of I appears to be due to a direct cytotoxic activity.

IT 87081-35-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(neoplasm inhibition by, mechanism of)

RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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L8            2 S L7 AND METALLOPROTEINAS?
L9          136 S L7 AND LEPTOMYCIN B
L10          55 S L9 AND PY<2002
L11           0 S L10 AND SKIN
L12           1 S L10 AND FUNGAL
L13           7 S L10 AND TUMOR

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